

08/878,454

CLAIMS

That which is claimed is:

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- Sub A1
1. A method to reduce induced apoptosis mediated by protein-protein interaction, the method comprising:

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inhibiting interaction of presenilin 2 comprising the amino acid sequence depicted in SEQ ID NO: 1 with a calcium-binding myristoylated protein having an homology to calcineurin comprising the amino acid sequence depicted in SEQ ID NO: 2.

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2. The method according to claim 1, wherein the presenilin 2 is a human protein.

3. The method according to claim 2, wherein the calcium-binding myristoylated protein is a human protein.

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- Sub A2
4. The method according to claim 3, wherein the calcium-binding myristoylated protein has reduced interaction with presenilin 1 having the amino acid sequence depicted in SEQ ID NO: 3 relative to the interaction with presenilin 2.

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5. The method according to claim 3, wherein inhibiting the interaction between the presenilin 2 and calcium-binding protein is facilitated by substitution of amino acid residue at 287, 288 and/or 297 of SEQ ID NO: 1.

- Sub B1
6. The method according to claim 5, in which the proline residue at position 287 is substituted by threonine.

7. The method according to claim 5, in which the alanine residue at position 297 is substituted by threonine.
8. The method according to claim 3, wherein inhibiting the interaction between the presenilin 2 and calcium-binding protein is facilitated by substitution of at least one amino acid residue in the calcium-binding EF-hands of SEQ ID NO: 2, wherein the calcium-binding hands including amino acid residues at positions 116 to 128 and 161 to 173 of SEQ ID NO: 2.
9. The method according to claim 8, wherein at least one acidic residue in the EF-hands is substituted with its amine counterpart.
10. The method according to claim 8, wherein at least one N-terminal residue is substituted at a position 1 to 3 of SEQ ID NO: 2.
11. The method according to claim 10, wherein an N-terminal glycine is substituted by alanine.
12. A substantially pure mutant calcium-binding protein comprising SEQ ID NO: 2 having a substitution of at least one amino acid residue in at least one calcium-binding EF-hand of SEQ ID NO: 2.
13. An isolated and purified nucleic acid molecule encoding a mutant calmyrin protein of SEQ ID NO: 2, the mutant protein comprising an amino acid residue substitution at position 2, 127 and/or 172 of SEQ ID NO: 2.
14. An expression vector comprising the nucleic acid molecule of claim 13.
15. A host cell transformed with the expression of vector of claim 14.

- Sub B1
16. The expression vector according to claim 14, wherein the amino acid substitution is selected from the group consisting of G2A, D127N, and E172Q.
- Sub A4
- 5 17. A substantially pure mutant calcium-binding protein comprising SEQ ID NO: 2 having a substitution of at least one amino acid penultimate N-terminal residue is substituted.
- 10 18. An isolated and purified nucleic acid molecule encoding a mutant of human presenilin 2 protein (SEQ ID NO: 1), the mutant comprising amino acid substitutions at positions 287, 288 and/or 297 of SEQ ID NO: 1.
- 15 19. An expression vector comprising the nucleic acid molecule of claim 18.
- 20 20. A host cell transformed with the expression of vector of claim 18.
21. The host cell according to claim 20, wherein the host cell is a bacterial cell, insect cell, plant cell or animal cell.
22. The expression vector according to claim 18, wherein the amino acid substitution is selected from the group consisting of P287T, I288L and A298T.
- 25 23. A method of reducing apoptosis in neuronal cells comprising:
administering a calcium-binding myristoylated protein having an homology to calcineurin comprising the amino acid sequence depicted in SEQ ID NO: 2 in a sufficient amount to effect protein-protein interaction with presenilin 2 comprising the amino acid sequence depicted in SEQ ID NO: 1, wherein the amino acid sequence depicted in SEQ ID NO: 2 contains substitution in the amino acid residues in the calcium-binding EF-hands and/or in a penultimate N-terminal residue.
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- ADD A6